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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/669,251	09/25/2003	Leland Shapiro	SHAP 000120	3193
68514	7590	01/09/2008	EXAMINER	
Don D. Cha 547 Buena Vista Road Golden, CO 80401			KWON, BRIAN YONG S	
		ART UNIT		PAPER NUMBER
		1614		
		MAIL DATE		DELIVERY MODE
		01/09/2008		PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	10/669,251	SHAPIRO, LELAND
	<b>Examiner</b>	<b>Art Unit</b>
	Brian S. Kwon	1614

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 05/30/07.
- 2a) This action is FINAL.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 25-30 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 25-30 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 09/25/2003 is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:
  1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

1. The examiner for the instant application has changed. The current examiner assigned to this application is Brian-Yong S. Kwon. Claims 25-30 are presented for examination.

### ***Response to Arguments***

2. Applicant's arguments with respect to claims 25-30 have been considered but are moot in view of the new ground(s) of rejection.
3. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of actions being applied to the instant application.

### ***Claim Objections***

4. Claim 28 is objected to because of the following informalities: "One of heart..." in claim 28 should be corrected as "one of heart...", respectively.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 25-30 are rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims 25-30 are directed to encompass "alpha1-antitrypsin-like agent" which only correspond in some undefined way to specifically instantly disclosed chemicals. None of these meet the written description provision of 35 USC 112, first paragraph, due to lacking chemical structural information for what they are and chemical structures are highly variant and encompasses a myriad of possibilities. To the extent that no structure function data is disclosed in connection with these functionally described compounds to correlate, or there is not disclosed correlation established between these functional drugs and the contemplated desired therapeutic effect to be achieved in practicing the instant invention, the specification provides insufficient written description to support the genus encompassed by the claims.

Vas-Cath Inc. Mahurkar, 19 USPQ2d 1111, makes clear the "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

With the exception of alpha1-antitrypsin, the skilled artisan cannot envision the detailed chemical structure of the encompassed derivatives, analogs, etc., regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad

class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966(1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

#### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 25-30 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 00/51623.

WO'623 (which contains the same disclosure or specification as the instant application) teaches a use of at least one of serine protease inhibitor such as alpha1-antitrypsin, alpha1-antitrypsin-like agent, antielastase, antiproteinase-3 agent or (benzyloxycarbonyl)-L-valyl-N-[1-

(3-(5-3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl-2-(5)-methylpropyl]-L-prolinamide in combination with at least one free radical scavenger such as 2,6,8-trihydroxypurine and dihydrorhodamine for the treatment of pathological conditions related to excess NO including ischemia-reperfusion injury (see abstract; page 1, lines 7-12; page 5, lines 30-31; page 6, lines 19-27; page 8, lines 4-6; page 9, line 6 through page 13, line 23; page 14, line 23 through page 15, line 10; Table 1; page 17, lines 11-34; page 18, lines 24-26; page 19, lines 18-22; Examples 6.3). WO'623 also teaches the instantly required "thrombolytic agent" in claim 26; "a mechanical device to reestablish blood flow" in claim 27; "the ischemia reperfusion injury is associated with at least one of heart, brain, lung, kidneys or liver" in claim 28; "the alpha1-antitrypsin-like agent is a form of alpha1-antitrypsin resistant to inactivation by oxygen reactive intermediates" in claim 29; and "the mechanical device involves percutaneous transluminal coronary angioplasty or angioplasty" in claim 30.

***Claim Rejections - 35 USC § 103***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. Claims 25-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gyorkos et al. (USP 5618792) in view of Wikberg et al. (USP 6599943), and further in view of Neuwelt et al. (US Patent Application Publication No. 2004/013666), Verstraete (European Heart Journal, Vol. 6, pp. 586-593, 1985) and/or Woods (USP 5180366).

Gyorkos teaches substituted oxadiazole, thiadiazole and triazole peptoids, which are useful as inhibitors of serine proteases including human neutrophil elastase (elastase inhibitory activity). Note the examples I-XVI are the same compounds of disclosed in applicants' claim 1. Note particularly column 7, lines 58-67 and column 8, lines 1-67 teaches the instant compounds are formulated into pharmaceutical compositions. Column 7, lines 45-57 teaches the instant compounds are used to treat various diseases such as myocardial ischemia/reperfusion or other conditions disclosed in column 1, lines 28-42.

Wikberg teaches use of free radical scavenger (i.e., 2,6,8-trihydroxypurine (uric acid) and N-acetyl-cysteine) in combination with hydroxyguanidines (column 11, line 26 and claim 8) for the treatment of ischemia-reperfusion injury including heart infarction (abstract; column 3, lines 9-63; column 5, lines 25-32; column 9, lines 20-27).

Neuwelt, Verstraete and Woods are being supplied as supplemental references to demonstrate the art recognition in using free radical scavengers for the treatment of ischemia-reperfusion injury associated with heart, brain, lung, kidneys or liver of ordinary skill in the art (abstract; para. [0025]-[0028] of US PG PUB 2004/0132666); using a thrombolytic agent such as streptokinase to treat an ischemia reperfusion injury such as myocardial infarction (abstract of

European Heart Journal, Vol. 6. pp. 586-593, 1985); and using an apparatus used to reestablish blood flow in a patient that involves angioplasty.

The teaching of Gyorkos differs from the claimed invention (i) mainly in the use of said serine protease inhibitors in combination with free radical scavenger such as 2,6,8-trihydroxypurine (uric acid) for the treatment of ischemia reperfusion injury, (ii) "thrombolytic agent" as the additional agent (claim 26), (iii) "additionally comprising using a mechanical device to re-establish blood flow" (claim 27) and (iv) "the mechanical device involves percutaneous transluminal coronary angioplasty or angioplasty" (claim 30).

Above references in combination make clear that said serine protease inhibitor and said free radical scavenger have been individually used for the treatment of ischemia reperfusion injury. It is obvious to combine two compositions each of which is taught by prior art to be useful for same purpose; idea of combining them flows logically from their having been individually taught in the prior art. The combination of active ingredient with the same character is merely the additive effect of each individual component. See *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980).

With respect to the incorporation of thrombolytic agent, one skilled in the art would have expected as taught by combination of Gyorkos, Wikberg, Neuwelt and Verstraete that the combination of individual agents known to treat ischemia reperfusion injuries into a single composition would give an additive effect in the absence of evidence to the contrary. Moreover, combining agents which are known to be useful for the treatment of ischemia and reperfusion individually into a single composition useful for the very same purpose is *prima facie* obvious. See *In re Kerkhoven* 205 USPQ 1069.

With respect to the incorporation of a mechanical device for reestablishing blood flow (e.g., percutaneous transluminal coronary angioplasty or angioplasty), one having ordinary skill in the art would have expected as taught by combination of Gyorkos, Wikberg, Neuwelt and the combination of individual agents known to treat ischemia reperfusion injuries into a single composition would give an additive effect in the absence of evidence to the contrary. Moreover, combining agents which are known to be useful for the treatment of ischemia and reperfusion individually into a single composition useful for the very same purpose is *prima facie* obvious.

See *In re Kerkhoven* 205 USPQ 1069.

Although the instant claims use the different names for the said ingredients than those taught in the cited references, these references are particularly pertinent and relevant because all the claimed species and their roles are well taught in the cited reference. Thus, one would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

### Conclusion

8. No Claim is allowed.
9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system, see <http://pair-direct.uspto.gov> Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Brian Kwon  
**Primary Patent Examiner**  
**AU 1614**

